

factor. As the claims now exclude intact LF, Applicants respectfully request that the rejection be withdrawn.

Rejection under 35 USC 112, first and second paragraph: indefiniteness and written description

Claims 1-7 were rejected as allegedly indefinite and lacking written description for reciting "anthrax protective antigen binding protein," which is defined in the specification as encompassing binary toxin functional equivalents. Applicants have amended claim 1 to recite that the LF and PA proteins of the invention are from *B. anthracis*. Applicants therefore respectfully request that the rejection be withdrawn.

Rejection under 35 USC 103: obviousness

The Examiner has rejected claims 1-7 as allegedly obvious over Leppla *et al.*, which teaches the use of anthrax protective antigen and fusion proteins comprising LF. As noted by the Examiner, Leppla *et al.* does not teach the molar ratio stated in claim 1, but teaches that the amount of PA and LF fusion protein will be optimized using routine procedures. Applicants respectfully traverse.

The rejection has failed to establish a prima facie case of obviousness for the present application. In order to establish a prima facie case of obviousness, the rejection must demonstrate that (1) the cited references teach all the claimed elements; (2) there is a suggestion or motivation in the prior art to modify or combine the reference teachings; and (3) there is a reasonable expectation of success. MPEP § 2143; *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

Specifically, the rejection has failed specifically to identify the principles, known to one of ordinary skill in the art, that suggest the combination of claimed invention (*In re Rouffet*, 47 USPQ2d 1453 (Fed. Cir. 1998)). One skilled in the art would therefore lack motivation to select the specific ratio of PA to LF described in the claims (molar ratio of PA to LF fusion protein is greater than 1).

In the rejection, the Examiner concludes that the presently claimed invention would be obvious, without identifying the principles that would motivate one of skill in the art to combine the cited references. By using hindsight to provide the requisite motivation, the Examiner has failed to make a prima facie case of obviousness. *In re Rouffet*, 47 USPQ2d 1453 (Fed. Cir. 1998). As discussed by the Federal Circuit in *In re Rouffet*,

Because the Board did not explain the specific understanding or principle within the knowledge of a skilled artisan that would motivate one with no knowledge of Rouffet's invention to make the combination, this court infers that the examiner selected these references with the assistance of hindsight. This court forbids the use of hindsight in the selection of references that comprise the case of obviousness" (*In re Rouffet*, 47 USPQ2d at 1458).

The present invention is a selection invention, in which a particular ratio of PA to LF fusion protein is used in the claimed compositions. Although Leppla *et al.* generically discloses the composition of the invention, Leppla *et al.* is silent as to any particular ratio of proteins used in the composition. Leppla *et al.*, either alone or in combination, therefore fails to provide motivation to select this particular claimed ratio. Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Klimpel et al.
Application No.: 09/853,530
Page 5

PATENT

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

A handwritten signature in cursive script, reading "Annette S. Parent".

Annette S. Parent
Reg. No. 42,058

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300
ASP:dk
SF 1351436 v1

APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Please amend page 1, lines 8-9, as follows:

This application is a divisional application of US application 08/937,275, filed September 15, 1997, and claims the benefit of provisional application 60/025,270, filed September 17, 1996, herein each incorporated by reference in their entirety.

IN THE CLAIMS:

1. (twice amended) A composition capable of inducing an immune response in a mammal to cytotoxic T cell epitopes of a full length protein wherein the composition comprises a unit dose of [an] *Bacillus anthracis* anthrax protective antigen and said full length protein bound to an anthrax protective antigen binding protein, wherein the molar ratio of protective antigen to the full length protein bound to the anthrax protective antigen binding protein is greater than one, and wherein the anthrax protective antigen binding protein comprises at least about the first 250 amino acid residues of the lethal factor of *Bacillus anthracis* and less than all of the amino acid residues of the lethal factor.

APPENDIX B
PENDING CLAIMS

1. (twice amended) A composition capable of inducing an immune response in a mammal to cytotoxic T cell epitopes of a full length protein wherein the composition comprises a unit dose of [an] *Bacillus anthracis* anthrax protective antigen and said full length protein bound to an anthrax protective antigen binding protein, wherein the molar ratio of protective antigen to the full length protein bound to the anthrax protective antigen binding protein is greater than one, and wherein the anthrax protective antigen binding protein comprises at least about the first 250 amino acid residues of the lethal factor of *Bacillus anthracis* and less than all of the amino acid residues of the lethal factor.

2. (previously once amended) The composition of claim 1 wherein the protective antigen is a processed protective antigen.

3. (previously once amended) The composition of claim 1 wherein the composition is sterile.

4. (previously once amended) The composition of claim 1 wherein the composition further comprises physiologically compatible salts.

5. (previously once amended) The composition of claim 4 wherein the composition is in an aqueous solution of physiologically compatible salts.

6. (previously once amended) The composition of claim 1 wherein the anthrax protective antigen binding protein is the lethal factor of *Bacillus anthracis*.